ASTHMA DURING PREGNANCY

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Conflict of Interest

- Speaker's bureau: Teva and Merck

Outline

- Respiratory physiologic changes in pregnancy
- The effect of asthma on pregnancy & the fetus
- The effects of pregnancy on asthma control
- Asthma treatment decisions during pregnancy
  - Medications: FDA Pregnancy categories
  - Acute asthma during pregnancy
  - Immunotherapy and pregnancy
- Pregnancy-induced rhinitis

Pregnancy concerns: Case Study

- 30 yr-old F
- Asthma since college:
  - SABA prn, ICS/LABA, LTRA
- Food allergies: epi
- Allergic rhinitis:
  - Avoidance measures, INS, antihistamine
- I'M PREGNANT!!

Questions:

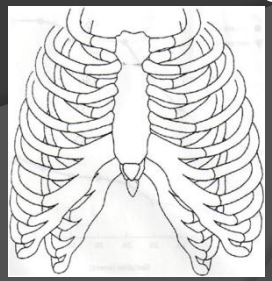
- Will my asthma get worse while I'm pregnant?
- Will having asthma effect my baby?
- Will the asthma medications hurt my baby?

Respiratory Changes: During Pregnancy

- Increased minute ventilation (same RR, ↑TV)
  - Increased respiratory drive: increased progesterone
  - First trimester. Increases 30%
- Compensated respiratory alkalosis
  - ($PaCO_2$ 40→32)
- Low expiratory reserve volume
- FVC and FEV1 are unchanged!
- Despite dramatic physical, hormonal alteration of pregnancy….lung function impact is minor!

Other changes during pregnancy

- Increased cardiac output & pulmonary blood flow
- Increased blood volume, but decreased hemoglobin
- Decreased plasma oncotic pressure (lower albumin)
- Increased circulating free cortisol
- Decreased chest wall compliance from enlarging uterus that increases abdominal pressure
- Diaphragm elevates 4 cm/lower rib cage increases
- Rib cage changes due to relaxin: progressive relaxation in ligaments, causes angle of ribcage to increase from 68º to 102º



Non-Asthma Respiratory Issues

- Physiologic Dyspnea of Pregnancy
  - Increased effort of breathing (short of breath)
  - Increased minute ventilation (normal RR <20)
  - Not abrupt or paroxysmal
  - At rest or with exertion
  - 75% of women have exertional dyspnea by 30 wks
  - Normal spirometry, ABGs (for preg) and ECHO
  - $PaCO_2$ of 40 mmHg not normal for pregnancy
  - Tx: aerobic exercise

Pregnancy: Asthma

- Asthma affects 8% of women during childbearing years
- Well-controlled asthma poses no risk to mother or fetus
- Poorly controlled asthma does!
  - Mother: hypertension, premature delivery, death
  - Fetus: increased risk of stillbirth, prematurity, low birth weight, low APGAR scores

What are the effects of pregnancy on asthma?

- 1/3 improve, 1/3 same, 1/3 worsen
- Women with severe asthma---worsen
- Women with mild asthma---improve
- Change is similar on successive pregnancies
- Attacks: more common 24-36 weeks

What are the effects of pregnancy on asthma?

- Intermittent asthma:
  - 4.5 x risk of hospitalization (2.3% → 11.3%)
- Persistent asthma:
  - 2.5 x risk of hospitalization (8% → 20.3%)
- During labor/delivery: 10%
- Changes return to pre-pregnancy in 3 months

Asthma treatment during pregnancy: Challenging!

- Avoidance measures
  - Smoking, allergens
  - Influenza vaccine
- Quick relief
- Daily controllers
  - ICS and ICS/LABA
  - Leukotriene modifier
- Allergy immunotherapy

FDA Pregnancy Category

- Potential to cause birth defects
- A Adequate/well-controlled studies failed to demonstrate risk to the fetus in 1st trimester of preg (no evidence of risk in later trimesters).
- B Animal studies failed to demonstrate a risk to fetus and there are no adequate/well-controlled studies in pregnant women
- C Animal studies shown adverse effect on fetus but no adequate/well-controlled studies in humans, but potential benefits may warrant use despite potential risks
- D Evidence of human fetal risk based on data from investigational or marketing experience or studies in humans, but potential benefits may warrant use despite potential risks
- X Studies (animals or humans) show fetal abnormalities and/or there is evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and risks clearly outweigh potential benefits.
- N Not classified by the FDA

Pregnancy Categories

- SABA: albuterol, terbutaline: less studied — C
- SAMA: Atrovent — B
- ICS/INS: — C
  - Budesonide — B
- ICS/LABA — C
- Cromolyn — B
- Montelukast and zafirlukast — B
  - Zilueton (Zyflo) — C
- Theophylline (5-12 mcg/mL) — C
- Prednisone — C
- Antihistamines — B
  - Fexofenadine — C
- Nasal antihist/Mast cell stab (patanase) — C
- Decongestant (oral): ? nasal — C
  - 1st trim: gastroschisis, small intestine atresia, hemifacial microsomia

Acute asthma during pregnancy

- Goals: prevent maternal and fetal hypoxia
- Similar to non-pregnancy
  - Rapid reversal of airflow obstruction
  - Reduce likelihood of recurrence
  - Ongoing assessment
- Oxygen
- SABA
- Systemic steroids

Human Studies: Theophylline

- 5 Selected studies: retrospective, cohort, database
- N=1875 exposed (on Theo)
- Not significant:

  Congenital anomalies, low birth weight, perinatal death, pre-eclampsia

  1 study showed 5% increased risk of pre-term delivery

Human Studies: SABA

- 5 Studies including Collaborative Perinatal Project
- N=5333, exposed to ephedrine, epi, albuterol, metaproterenol, terbutaline
- Not significant
  - Congenital anomalies, low birth weight, pre-term delivery, preeclampsia
  - (Too few subject to allow any conclusions for specific major birth defects)

Human Studies: LABA

- Limited data; 4 studies, 2 in UK.
- Prescription event monitoring
- N=234
- Number is too small for comparisons to general population.

Human Studies: LTRA (Singulair)

- Pregnancy Registry by Merck closed May 15, 2013.
- 1 in 180 births: malformation (less than the 1-3% in general population)
- Not significant
  - Low birth weight
  - Pre-term delivery
  - Major birth defects

Human Studies: Inhaled Steroids

- 6 cohort studies; Nearly 6500 exposed
- Mostly: beclomethasone, triamcinolone budesonide (n=>3000)
- No significant increase in:
  - Low birth weight
  - Preterm delivery
  - Major malformations
  - Preeclampsia

Human Studies: Oral Steroids

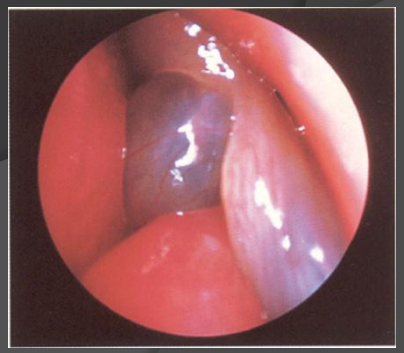
- 8 Studies, N=580 exposed
- Increased
  - preeclampsia (13% vs 7.5%); OR 2
  - Pre-term delivery; OR 1.54-3.37 (2.2 weeks)
  - Low birth weight; OR1.8
  - Birth defects: cleft lip/palate (4 case-control studies)
    - Use in 1st month: cleft lip: OR 5.9 (n=3; smoking not taken into account—independent risk factor for clefts)
    - Use in 1st trimester: OR 6.6 (n=5)
    - 3 month period around conception: OR 4.3-5.3 (n=9)
- So, if risk is causal: risk increases from 1 up to 3 per 1000 women if taken during embryogenesis.

Human Studies:
Allergen immunotherapy

- Not on immunotherapy: wait
- On immunotherapy: continue if experiencing clinical benefit and not having systemic reaction
  - Build-up: stop build-up
  - Maintenance: decrease slightly and maintain
- Risks: allergic reaction to IT injection
- Extracts: not considered a risk to fetus
  - (2 retrospective cohort studies during 1st trimester)

Rhinitis of pregnancy

- 22% of pregnant women
- Symptoms: congestion, watery, clear mucus in the last 6 or more weeks of pregnancy
- Not due to allergies, sinus, URI or overuse of nasal decongestants
- Snoring: increase risk of maternal hypertension, preeclampsia, IUGR and lower APGAR scores
- Risk factors: smoking, dust allergy

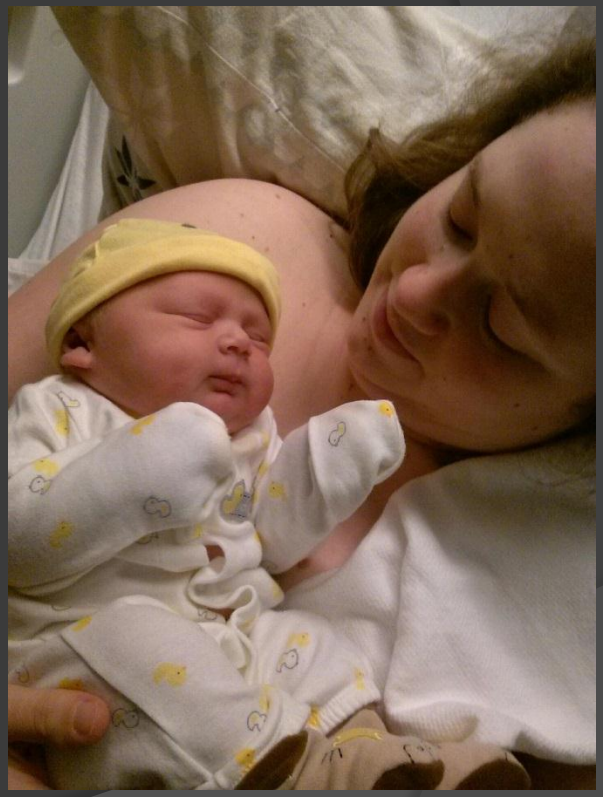


Rhinitis of Pregnancy: Treatment

- Pre-natal advice
- Exercise: decongestant effect
- Elevate HOB 30-45^{o}
- Mechanical device: “BreatheRight strip”
- Saline nasal wash
- Nasal decongestant: temporary (<3-5 days)
- No data: Oral decongestant, oral steroid
- No help: INS, antibiotic, nasal CPAP
- Deliver the baby (symptoms gone in 2 weeks)

Conclusion:

- Many unanswered questions
- Uncontrolled asthma: risky to mother and fetus
- Asthma medications:
  - Limited data. Generally safe especially after embryogenesis
- Pregnancy rhinitis:
  - don’t underestimate the significance



Thank you

Mother and baby are doing well!